



FIG. 1-1

human neutral Sphingomyelinase (NSM) Gene Sequence

1 ACCGCGGCGCGTCGCTGGAGAGTTTCGAGCCGCTAGCGCCCTGGAGCTCCCAACCATGAT
TGGCGCCGGCAGCGACCTCTCAAGCTCGGCGGATCGCGGGGACCTCGAGGGGTGGTACT
E I
61 AGCCCAACTTCTCCCTGCGACTGCGGATCTTCAACCTCAACTGCTGGTGAGTGCCTCTGC
TCGGGTGTAAGAGGGGACGCTGACGCCTAGAAAGTTGGAGTTGACGACCACCTCACGCAGACG
120
121 GGAGTGCGGTCTGGGGGGCCACCTTCCGTTTCGCACCCATGCAAGCCTTCCTCCCCCTATCCC
CCTCAGCCAGACCCCGGTGGAAGGCAAGCGTGGGTACGTCGGAAGGAGGGGGATAGGG
180
181 GCCCCACGATCTCAGGGTGTAAGGGAAAACCCGAACCTCCAAAGTCCACATCTGGCCCCAG
CGGGGTGCTAGAGTCCCACATCCCTTTTGGGCTTGGAGGTTTCAGGTGTAGACCGGGGTC
240
241 CGCCGGTGGTCCCAGCAGTCGCCTCCCTGCCCCGCTCTTCCCTTCCTTAGGGGGCATTCC
GCGGCCACCAGGGTCGTCAGCGGAGGGGACGGGGCGAGAAAGGGAAGGAAATCCCCGTAAAG
300
301 GTACTTGAGCAAGCACCGGGCCGACCGCATGAGGCGCCTGGGAGACTTTCTGAACCAGGA
CATGAACCTCGTTTCGTGGCCCGGCTGGCGTACTCCGCGGACCTCTGAAAGACTTGGTCT
E II
361 GAGCTTCGACCTGGCTTTTGCTGGAGGAGGTGAGATTGTGCAGCACGGTGC GGAACCCAGG
CTCGAAGCTGGACCGAAACGACCTCCTCCACTCTAACACGTCGTGCCACGCCCTTGGGTCC
420
421 CTGGGAGGAGGGACAGACCGTCCCACTGGGGAAAGACCAAGCAGGCATCCTCACCGCTTC
GACCCTCCTCCTGTCTGGCAGGGTGACCCCTTTCTGGTTCTGTCGTCGTCAGTGGCGAAG
480
481 CCTCAGGTGTGGAGTGAGCAGGACTTCCAGTACCTGAGACAGAAGCTGTACCTACCTAC
GGAGTCCACACCTCACTCGTCTCTGAAGGTCATGGACTCTGTCTTCGACAGTGGATGGATG
540
E III
541 CCAGCTGCAACACCACTTCCGGAGGTGAGAAGCCCACTGGCCTGAAGCCTGTTGTATCCC
GGTCGACGTGTGGTGAAGGCCCTCCACTCTTCGGGTGACCGGACTTCGGACAACAGTAGGG
600
601 AGGAGGCTCTTGGCCCTGCCAGCCCTTCCCTATCCTGCCTGCACTCTCCAGTCTCCTCCA
TCCTCCGAGAACCGGGACGGTCGGGAAGGGATAGGACGGACGTCGAGAGGTGAGAGGAGGT
660
661 GCCTCCTCTCCTCTGGATGTGAGAGAAGGAGAAGGGTGAACCAAGAAGGTCCTATGACT
CGGAGGAGAGGGAGACCTACACTCTCTTCTCTTCCCACTTGGTTCTTCCAGGATACTGA
720
721 TCAGCCCCCTTTCAGCTTTGTTTTCTGGCTGCCCTATACTCCTCCAAAGGCCGTCGCCTTG
AGTCGGGGAAACTCGAAACAAAAGACCGACGGGATATGAGGAGGTTTCCGGCAGCGGAAC
780
781 GTTCTAGGGCTAGTCCCAGCAGTAGAAAAAGAAAAAAATAGCTGATCAGAGCTGGAAGAC
CAAGATCCCGATCAGGGTCTGTCATCTTTTCTTTTTTTATCGAGTAGTCTCGACCTTCTG
840
841 AAGGGAGGGGAAGAAGGCTGGGTGTCTCTCCCTGTTTTTCTGGTTATTAAAGCAGGGCTTG
TTCCCTCCCCTTCTTCCGACCCACAGAGAGGGACAAAAAGACCAATAATTCGTCCCGAAC
900



FIG. 1-2

1861 CTCTCCCTCTCTTCTCCCCACATCCTAGCATGAGCCAATGATTCCCTTAGGGCTCTGAGG 1920
GAGAGGGAGGAAGTGGGGGTGTAGGATCGTACTCGGTTACTAAGGGAATCCCGAGACTCC
E VIII
1921 AAGGCAACACAATGGTACCCAAGAACTGNTACGTCAGCCAGCAGGAGCTGAAGCCACCCCT 1980
TTCCGTTGTGTTACCATGGGTCTTGACNATGCAGTCGGTCTGCTCCTCGACTTTCGGTGGGA
1981 CCTTTGGTGTCTCCGCATTGACTACGTGCTTTACAAGGTCAGGCTCCTCCCTTCAACATGCT 2040
GGAAACCACAGGCGTAACCTGATGCACGAAATGTTCCAGTCCGAGGAGGGGAAGTTGTACGA
2041 TTCATATGCTGTGTCTCTTTGTCTAACCTGTGTAGATCCTCCTTTGCTCAGNTAGTCTAG 2100
AAGTATACGACACAGAGAAACAGATTGGACACATCTAGGAGGAAACGAGTCNATCAGATC
2101 TCTTGGACCACCTGATGGGTGGAAAGTGGGGTAGCCGGGAGCTGGTTCTCTGGGAAGAGGC 2160
AGAACCTGGTGACTACCCACCTTTACCCCATCGGCCCTCGACCAAGAGACCCTTCTCCG
2161 CCTCATATATAAGCTTCTCTNTGGCCCTTACTTTTCCTAGGCAGTTTCTGGGTTTTACAT 2220
GGAGTATATATTTCGAAGAGANACCGGGAAATGAAAAGGATCCGTCAAAGACCCTAAAATGTA
2221 CTCCTGTAAGAGTTTTGAAACCACTACAGGCTTTGACCCTNACAGGGGGCACCCCCCTCTC 2280
GAGGACATTCTCAAAACTTTGGTGATGTCCGAAACTGGGANNTGTCCCGTGGGGGGAGAG
2281 TTGATCATGAAGCCCTGATGGCTACTCTGTTTGTGAGGCACAGCCCCCACAGCAGAACC 2340
AACTAGTACTTCGGGACTACCGATGAGACAAACACTCCGTGTCTGGGGGGTGTCTCTTTGG
2341 CCAGCTCTACCCACGGTGAGTCACCCCAACCTTTCTTGGCCCTTGCCCGGCTTGAAGC 2400
GGTCGAGATGGGTGCCACTCAGTGGGGGTGGAAAGGAACCGGGAACGGGGCGAAGTTCTG
2401 AGCCCTTCCACTCTTGA CTCTCTCCTGCCCACTGCCCTGCTCTGTGTAGGACCAGCAG 2460
TCGGGAAGGTGAGAACTGAGAGAGGACGGGGTGACGGGACGAGACAACATCCTGGTCTCTC
2461 AGAGGTCGCCGTTGATGTGTGTGCTAAAGGAGGCCCTGGACGGAGCTGGGTCTGGGCATGG 2520
TCTCCAGCGGCAACTACACACACGATTTCCTCCGGACCTGCCTCGACCCAGACCCGTACC
2521 CTCAGGCTCGCTGGTGGGCCACCTTCGCTAGCTATGTGATTGGCCTGGGGCTGCTTCTCTC 2580
GAGTCCGAGCGACCAACCCGGTGGAAAGCGATCGATACACTAACCGGACCCCGACGAAGAGG
E IX
2581 TGGCACTGCTGTGTGTCTCTGGCGGCTGGAGGAGGGGGCCGGGGGAAGCTGCCATACTGCTCT 2640
ACCGTGACGACACACAGGACCGCCGACCTCCTCCCCGGCCCTTCGACGGTATGACGAGA
2641 GGACCCCCAGTGTAGGGCTGGTGTGTGGGCAGGTGCATTCTACCTCTTCCACGTACAGG 2700
CCTGGGGGTACATCCCGACACGACACCCGTCCACGAAAGATGGAGAAGGTGCATGTCTC
2701 AGGTCAATGGCTTATATAGGGCCAGGCTGAGCTCCAGCATGTGTCTAGGAAGGGCAAGGG 2760
TCCAGTTACCGAATATATCCCGGGTCCGACTCGAGGTCTGTACACGATCCTTCCCGTTCCC
2761 AGGCCCAAGGATCTGGGCCCAAGAGCCTCAGCCAGCCCTACTCCTGGGGCAGCAGGAGGGGG 2820
TCCGGGTGGTAGACCCGGGTCTCGGAGTCGGTCCGGATGAGGACCCCGTCTCTCTCCCC

ACAGAACTAAAGAACAATAAAGCTTGGCCCAA



FIG. 1-3

2821 T G T C T T G A T T T C T T G T T A T T T C G A A C C G G G T T 2852



FIG. 2-1

Mouse Neutral Sphingomyelinase (nSMase) gene sequence

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1  TNGANNCTGTTAGCTCCAGNCCGGTNGGTGCGCGTNCTAGNCNNATCTNTATAGCTCTTC 60
   ANCTNNGACAATCGAGGTCNGGCCANCCAGCGGCANGATCNGNNTAGANATATCGAGAAG
61  GTTGCGAGCNCAATTNNNTCTCAATAAANGGATNCANCCCTATGACAGAACGTGGACCCC 120
   CAACGCTCGNGTTAANNNAGAGTTATTTNCCTANGTNGGGATACTGTCTTGCACCTGGGG
121 CGCCCGCCANCNCANGNGANACCGCGGCATGGGNCTGAGGTGCNCANGGTGTCTGGGGCG 180
   GCGGGCGGTNGNGTNCNCTNTGGCGCCGTACCCNGACTCCACGNGTNCCACAGACCCCGC
181 AGGGGTTACCTCAGCGATGGTCTTTGACACCTGAAAGCTGGAGCTTTTGAANAGCCCCAN 240
   TCCCCAATGGAGTCGCTACCAGAACTGTGGACTTTTCGACCTCGAAAACCTTNTCGGGGTN
241 CACCTTCAGCTTCAGGGGCGGCTCNGGCGGCAACCGCACGTGANATGCTGGGGGCTTCGA 300
   GTGGAAGTCGAAGTCCCCGCCGAGNCCGCCGTTGGCGTGCACTNTACGACCCCCGAAGCT
301 CTTGGGCGCGGCACGGNTGCTGGGTGGCCATGGAANNNNACAGNACAGAGCCGGNACACAA 360
   GAACCCGGCGCGTGCCNACGACCCACCGGTACCTTNNNTGTCNTGTCTCGGCCNTGTGT
361 ATANTGCGAGTCGCCANGGNAACCGCGTGGCTCCTCCCCGAACGCCCNCAAGGGGCGGGA 420
   TATNTCGCTCAGCGGTNCCNTTGGCGCACCGAGGAGGGGCTTGGCGGNGTTCCCCGCCCT
421 CCTGAGTGAGTTTCNTGGGCGGGGCTCNCATCAACTTCAAGCCTGTTGCTGGTGGAAAGCC 480
   GGACTCACTCAAGNACCCGCCCGGAGNGTAGTTGAAGTTGGGACAACGACCACCTTCGG
481 GAGCCGGGAACAAGGGAGGAACCTGTAGGCCGCGGTGCGGATAACCCACCGAAGGACCTA 540
   CTCGGGCCCTTGTTCCTCCTTGGACATCCGGCGCCACGCCCTATTGGGTGGCTTGGTGGAT
E I
541 AGAATCTGGAACAGTCCACCCGAGATTCTTCCAGGACTGCCGGCGGGACTCTCGCATTC A 600
   TCTTAGACCTTGTCAAGGTGGGCTCTAAGGAAGGTCCTGAGGGCCGCCCTGAGAGCGTAAGT
601 GCCCGGGATTTGCGAGCCGACCTTCTTTCCGGGTGGAATGACGGCCTTTGTCCCAGTAACG 660
   CGGGCCCTAAACGTCGGCTGGAAGAAAGGCCACCTTACTGCCGGAAACAGGGTCATTGC
661 CAGGAGTCNNCCCCACCCCCAACCAGCTCGCGTTCCTGGGTGCGGGGCAGCGCAGGATAGG 720
   GTCCTCAGNNGGGGTGGGGGTGGTTCGAGCGCAAGGACCCAGCCCCGTCGCGTCCTATCC
                                                                Start
721 GCATAAGCCTGTGCGCGCAAATCCGCCCTCGCCGCCCTTGCTCCGAAGCACTCCAGCCATG 780
   CGTATTCCGGACACGCGCGTTTAGGCGGAGCGGCGGGAACGAGGCTTCGTGAGGTCGGTAC
781 AAGCTCAACTTTTCTCTACGGCTGAGAGTTTTCAATCTCAACTGCTGgtgagtgagtgagtgct 840
   TTCGAGTTGAAAAGAGATGCCGACTCTCAAAAGTTAGAGTTGACGACcattcattcacga
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FIG. 2-2

841 c c c a g g c g t g g g c t g c a g c c t c g g a g c c a c c t t c c a g t c c c t c t c g c a c a t g c c t a g g a 900
g g g t c c g c a c c g a c g t c g g a g c c t c g g t g g a a g g t c a g g g g a g a g c g t g t a c g g a t c c t

901 a g g a a g c a g g t c t t c t t c a g c c g a g c t a g a c c c t g t c c t t c c c g a a c c a c c a a a g t c c a c 960
t c c t t c g t c c a g a a g a a g t c g g c t c g a t c t g g g a c a g g a a g g g c t t g g t g g t t t c a g g t g

961 a t c g c c t a a a g a c c a g a g c t t g g g t g g t t g c a g c a a t c a c c a a a g t c c c t a t c a t c c a a a 1020
t a g c g g a t t t c t g g t c t c g a a c c c a c c a a c g t c g t t a g t g g t t t c a g g g a t a g t a g g t t t

1021 g c t g a g g t g a t g a c a g c a g t a a t c g t c c c a a a c c t g g c c c a t g t c t t t c c t t t t a a a t g a 1080
c g a c t c c a c t a c t g t c g t c a t t a g c a g g g t t t g g a c c c g g t a c a g a a a g g a a a a t t t a c t

1081 t t t a c t t t t a t t t t a t g t a c a t t t g g t g t t t t g c c t g t a t g t a t g t c t g t g t g a a g g t g c 1140
a a a t g a a a a t a a a a t a c a t g t a a a c c a c a a a a c g g a c a t a c a t a c a g a c a c a c t t c c a c g

1141 c a g a t t c t c t g g a a c t g g a g t t a c a g a c a g t t g t a a g c t g t c a t g t g c t t g c t g g a a a t t 1200
g t c t a a g a g a c c t t g a c c t c a a t g t c t g t c a a c a t t c g a c a g t a c a c g a a c g a c c t t t a a

1201 g a a c t g c t g a c c c a t c t c t t c t g c c c c c t g c g t c c t c c a c c c t t t t a g g g a c a t c c c c t 1260
c t t g a c g a c t g g g t a g a g a a g a c g g g g g a c g c a g g a g g t g g g g a a a a t c c c t g t a g g g g a

1261 a c c t g a g c a a a c a t a g g g c g g a c c g c a t g a a g c g c t t g g g a g a c t t t c t g a a c t t g g a a a 1320
t g g a c t c g t t t g t a t c c c g c c t g g c g t a c t t c g c g a a c c c t c t g a a a g a c t t g a a c c t t t

E II

1321 a c t t t g a t c t g g c t c t c c t g g a g g a g g t g a g g t t g t a g g g c a g g c t a g g t t g g a g g a g g g 1380
t g a a a c t a g a c c g a g a g g a c c t c c t c c a c t c c a a c a t c c c g t c c g a t c c a a c c t c c t c c c

1381 c a g c a g g c g g c a g g c g g c g g c a g g a a a c t t g t t c t g t c t t g g g a t g a a a t c c c a a g c a a 1440
g t c g t c c g c c g t c c g c c g c c g t c c t t t t g a a c a a g a c a g a a c c c t c c t t t a g g g t t c g t t

1441 g t a t c c t c a c c t t c t t c c t c c a g g t g t g g a g t g a g c a g g a c t t c c c a g t a c c t a a g g c a a 1500
c a t a g g a g t g g a a g a a g g a g g t c c a c a c c t c a c t c g t c c t g a a g g g t c a t g g a t t c c g t t

E III

1501 a g g c t a t c g c t c a c c t a t c c a g a t g c a c a c t a c t t c a g a a g g t g a a a a g c c t g t g t t c t c 1560
t c c g a t a g c g a g t g g a t a g g t c t a c g t g t g a t g a a g t c t t c c a c t t t t c g g a c a c a a g a g

1561 a g c c t g t t c t c a g a c g a g g a a g c t c t c c a a c a t t c t t g c t t g c a c c c t c g a t c t t c t t c c 1620
t c g g a c a a g a g t c t g c t c c t t c g a g a g g t t g t a a g a a c g a a c g t g g g a g c t a g a a g a a g g

1621 t c t g g g t c t g a g a a g a g c a g g c c g t c a c c c t c a t c t t g c a a g g g c t g c t g t c t t a g g c t t 1680
a g a c c c a g a c t c t t c t c g t c c g g c a g t g g g a g t a g a a c g t t c c c g a c g a c a g a a t c c g a a

1681 t g t t c t g g g g t t g a t c t t a g c a g t a g a g c t g g g a g a c c g c g g a g g g g a a g a g g g c t g g c t 1740
a c a a g a c c c c a a c t a g a a t c g t c a t c t c g a c c c t c t g g c g c c t c c c c t t c t c c c g a c c g a



FIG. 2-3

1741 GGGTACTCCCCTCCTTGCTCTTCTGGTTATTAAAGCAAGAGTTGGTTTTTCAGCGGGATGAT 1800
CCCATGAGGGGAGGAACGAGAAGACAAATAATTCTGTTCTCAACCAAAGTCGCCCTACTA

E IV

1801 AGGCAGTGGCCTCTGTGTGTTCTCCAAACACCCCAATCCAGGAAATCTTCCAGCATGTCTA 1860
TCCGTCACCGGAGACACACAAGAGGTTTGTGGGTTAGGTCCTTTAGAAGGTCGTACAGAT

1861 CAGTCTGAATGGTTACCCCTACATGGTAAGGATCTCTTCCCTATCCTTGCTAACACAGAC 1920
GTCAGACTTACCAATGGGGATGTACCATTCCTAGAGAAGGGATAGGAACGATTGTGTCTG

1921 TGGACGCAGCCTTCCCTGGGGCCTTGGCAGGAGGGTGTCAGTACCCTGAGTTTTTGTCTTC 1980
ACCTGCGTCGGAAGGACCCCGGAACCGTCTCCACAGTCAATGGGACTCAAAAACAGAAG

1981 TCTTGCCTGCAGTTCATCATGGAGACTGGTTCTGTGGGAAGTCTGTGGGGCTGCTGGTG 2040
AGAACGGACGTCAAGGTAGTACCTCTGACCAAGACACCCCTCAGACACCCCGACGACCAC

E V

2041 CTCCGTCTAAGTGGACTGGTGCTCAATGCTACCGTGACTCATGTGAGTGGGGCTAGCCAG 2100
GAGGCAGATTACCTGACCACGTGTTACGATGGCACTGAGTACACTCACCCCGATCGGTCT

2101 GCTTAGGCAGTGGGTCAAGCAGCCCAATGCTATGGTGGAGAAGAGACGCCACTAGTTAGT 2160
CGAATCGGTACCCAGTTCTCGGGTTACGATACCACCTCTTCTCTGCGGTGATCAATCA

2161 TCTGCTGCCCTGGGGATAAGGCATGGGATCAGAAGCTAGCATTTGGGCAAGGTTACCCATT 2220
AGACGACGGACCCCTATTCCGTACCCTAGTCTTCGATCGTAACCCGTTCCAAGTGGGTAA

2221 CCCTGTCACACTCTGCCATGTGACAGATGACAAGCTTGATTCAGACAGCCTTCTCTTTGA 2280
CCCACAGTGTGAGACGGTAGACTGTCTACTGTTTGAAGTCTGTCGGAAGAGAACT

1281 TTTCACCTATTCCACTTTAGCTACATGCTGAGTACAGCCGACAGAAGGACATCTACTTTG 2340
AAAGTGGATAAAGGTGAAATCGATGTACGACTCATGTGCGCTGTCTTCTGTAGATGAAAC

E VI

2341 CACACCGTGTGGCCCAAGCTTGGGAACTGGCCCAAGTTTCAATCCAGTGTGTGAGCCTGGGGCT 2400
GTGTGGCACACCGGGTTTGAACCCCTTGACCGGGTCAAGTAGGTCACACACTCGGACCCGA

2401 TGATGGGGGCTGTGGGGTGGGGACGGGGTTGAGGGATGNGNAANTTATCCTTGAAGAGGG 2460
ACTACCCCCGAGTCCCCACCCCTGCCCCAACCTCCCTACNCNTTNAATAGGAACCTTCTCCC

2461 CACATAATAAGGGAAGAATTTCTCTCCTTGCCGCTCTTCCCCCAACTCAGCCACACATCCA 2520
GTGTATTATTCCCTTCTTCCCGGAGGAACGGCGAGAAGGGGTTGAGTGGGTGTGTAGGT

E VII

2521 AGAATGCAGATGTGGTTCTATTGTGTGGAGACCTCAATATGCACCCCAAAGACCTGGGGCT 2580
TCTTACGTCTACACCAAGATAAACACACCTCTGGAGTTATACGTGGGGTTTCTGGACCCGA



FIG. 2-4

2581 GCTGCCTGCTGAAAGAGTGGACAGGGCTCCATGATGCTTTCGTTGAGACTGAGGACTTTA 2640
CGACGGACGACTTTCTCACCTGTCCCGAGGTACTACGAAAGCAACTCTGACTCCTGAAAT

2641 AGGTGAGAGACTGTTTCCCACTCACTTGTTCAGTCTTCTCTTAGCAT 2700
TCCAGTCTCTCACAAAGGGTGGTTGAGGTGTGAACAAGGTGAGAAAGGACAGAGAATCGTA

2701 CCTAGCCACCTGTTTCCCTAGGGCTCTGATGATGGCTGTACCATGGTACCCAAGAAGTGC 2760
GGATCGGTGGACAAAGGGATCCCGAGACTACTACCGACATGGTACCATGGGTCTTGACG

E VIII

2761 TACGTCAGCCAGCAGGACCTGGGACCGTTTCCGTCTGGTATCCGGATTGATTACGTGCTT 2820
ATGCAGTCGGTCGTCTGGACCTGGCAAAGGCAGTCCATAGGCCTAACATAATGCACGAA

2821 TACAAGGTCAGGCTCTTATTTCCCGGTGTGCCTTCTCCAGTATCTTCTTCTCTGTCACT 2880
ATGTTCCAGTCCGAGAATAAGGGCCACACGGAAGAGGTCA TAGAAGGAAGGAGACAGTGA

2881 AGCCACAGCTTTAGTTCAGCTACAGTCTTGGGCCACTGATGGCTAAAGAATAGAATCCTG 2940
TCGGGTGCGAAAGCAAGTCGATGTCAGAACCCGGTGACTACCGATTTCTTATCTTAGGAC

2941 TCGGCTGGTCTCTGCGGAGAAATTTAAGCTTCTCCATGTTCTTGCTCTTCTAGGCAGTCT 3000
AGCCGACCAAGAGACCCTCTTAAATTGCAAGAGGTACAAGAACGAGAAGGATCCGTCAGA

3001 CTGAGTCCACGCTCTGCTGTGAGACTCTGAAAACCACTACAGGCTGTGACCTCAGAGTG 3060
GACTCAGGGTGCAGACGACACTCTGAGACTTTTGGTGATGTCCGACACTGGGAGTGTCAC

E IX

3061 ACAAGCCCTTCTCTGATCACGAGGCCCTCATGGCTACTTTGTATGTGAAGCACAGCCCCC 3120
TGTTGCGGAAGAGACTAGTGCTCCGGGAGTACCGATGAAACATACACTTCGTGTGCGGGG

3121 CTCAGGAAGACCCCTGTACTGCCTGTGGTAAGCAGCATTTCTTTGCCCCCTCTACTTTA 3180
GAGTCCTTCTGGGGACATGACGGACACCAATTCGTGCTAAAGGAAACGGGGGAGATGAAAT

3181 AGGCAGCCCCGCTCCATCCTGACCCTCCCTGCTCTACGTTCTCTCTTTTCCAGGCCC 3240
TCCGTCGGGGCGGAGGTAGGACTGGGAGGGGACGAGATGCAAGAGAGAAAAAGGTCCGGG

3241 ACTGGAAAGGTCCGATTTGATCAGCGTGCTAAGGGAGGCCAGGACAGAGCTGGGGCTAGG 3300
TGACCTTTCCAGGCTAAACTAGTCGCACGATTCCCTCCGGTCTGTCTCGACCCCGATCC

E X

3301 CATAGCTAAAGCTCGCTGGTGGGCTGCATTCTCTGGCTATGTGATCGTTTGGGGGCTGTG 3360
GTATCGATTTCGAGCGACCTCCCGACGTAAGAGACCGATACACTAGCAAACCCCGACAG

3361 CCTTCTGGTGTGCTGTGTGTCCTCCGGCTGCAGGAGAAGAGGCCAGGGAAGTGGCCATCAT 3420
GGAAGACCACAACGACACACAGGGCCGACGTCCTCTTCTCCGGTCCCTTTACCGGTACTA



FIG. 2-5

3421 CCTCTGCATACCCAGTGTGGGTCTGGTGTCTGGTAGCAGGTGCAGTCTACCTCTTCCACAA 3480
GGAGACGTATGGGTACACCCAGACCACGACCATCGTCCACGTACAGATGGAGAAGGTGT

3481 GCAGGAGGCCAAGGGCTTATGTCGGGGCCAGGCTGAGATGCTGCACGTTCTGACAAGGGA 3540
CGTCCTCCGGTTCGCCGAATACAGCCCGGGTCCGACTCTACGACGTGCAAGACTGTTCCCT

3541 AACGGAGACCCAGGACCGAGGCTCAGAGCCTCACCTAGCCTACTGCTTGCAGCAGGAGGG 3600
TTGCCCTCTGGGTCTGCTCCGAGTCTCGGAGTGGATCGGATGACGAACGTCGTCTCTCC

stop

3601 GGACAGAGCTTAAGAGCTTAACAATAAACTTTGCTTGACACACTCTAGTGGCTCTACCTT 3660
CCTGTCTCGAATTCTCGAATTGTTATTTTGAACGAACGTGTGTGAGATCACCGAGATGGAA

3661 GTTCCTTGCAGAGGCATGATGGGAAGTGAAGGTCAGTGGCCTTGTCACTGTGTGGCTTTA 3720
CAAGGAACGTCTCCGTACTACCTTGACTTCCAGTCACCGGAACAGTGACACTCCGAAAT

3721 GAGCGTTGGCCTCTCACTTGCCTTTTTTGCACACTCCCGTCTCCTGCCAGCACAGAGCAT 3780
CTCGCAACCGGAAAGTGAACGGAAAAAACGTGTGAGGGCAGAGGACGGTCTGTCTCTCGTA

3781 AAACCTGTTCATGGTCATAATCCTTTTTATTGTAAACAACGAAGCCTCTGACTAAGCAGT 3840
TTTGGGACAAGTACCAGTATTAGGAAAAATAACATTTGTTGCTTCGGAGACTGATTGGTCA

3841 CCAGATGGCGGAGGTACAGCCCTTGTGATGGTGTCTTGCCTTACGGGGCAGGGAGGCAGCT 3900
GGTCTACCGCCTCCATGTCGGGAACACTGCGACAGAACGAATGCCCGTCCCTCCGTCTGA

3901 AACCATCATCTTCTAGCCCTGGGCTCCCATCTATGCAGGCATCTCTCTGAGCCTCCGTTC 3960
TTGGTAGTAGAAGATCGGGACCCGAGGGTAGATACGTCCATCTAGAGACTCGGAGGCAAG

3961 CTCCTGGAATTGGNTCAGAGCAATCCCGCTTGGTTACCAACCTCCAAACAGCTTCTCTTA 4020
GAGGACCTTAAGGNAGTCTCGTTAGGGCGAACCAAGTGGGTGGAGGTTTGTCTCGCTTCT

4021 AGGACCTGGTTTTCTCAAAANGGNAAGGTNCGGGCCTCCGGTCTTCAATANGTTTTCTTAA 4080
TCCTGGGCCAAAGAGTTTTNCCNTTCCANCGGGGGTGGCCAGAAGTTATNCAAAAGGATT

4081 AAAGGGANGAATGAAAANCCTTAAGNNCCAACAAGGGGAACCTTGGNCCCAAAAGGGGA 4140
TTTCCCTNCTTACTTTTNGGAATTCNNGGTGTTCCTTGGGAACCNNGGTTTTTCCCT

4141 CCTGGGTGGTTTTCCCNNTTGGGGCCAAANTTATCCCAAAGGGGTCCAATTGAAGGGTTAAC 4200
GGACCCACCAAAAGGGNAACCCCGGTTTNAATAGGGTTTCCCACCTTAACCTTCCCAATTG

4201 CCCCCAAAAANNACCCNTTCCCCCGGAATTTCCAAAGGTTTNNCCCCCCCCGGGCAAAANC 4260
GGGGGTTTTTNNTTGGGNAAGGGGGCTTAAAGGTTTCCAANGGGGGGGGCCGTTTTNG



FIG. 2-6

4261 TCCCTTGGGGNNCCNAANCCNTGGCCCGGNCTTGGCTTTTCCCCCTTTCCCAAGNATTTCT 4320
AGGGAACCCCNNGGNTTNGGNACCGGGCCNGAACCGAAAAGGGGGAAAGGGTTTCNTAAAG

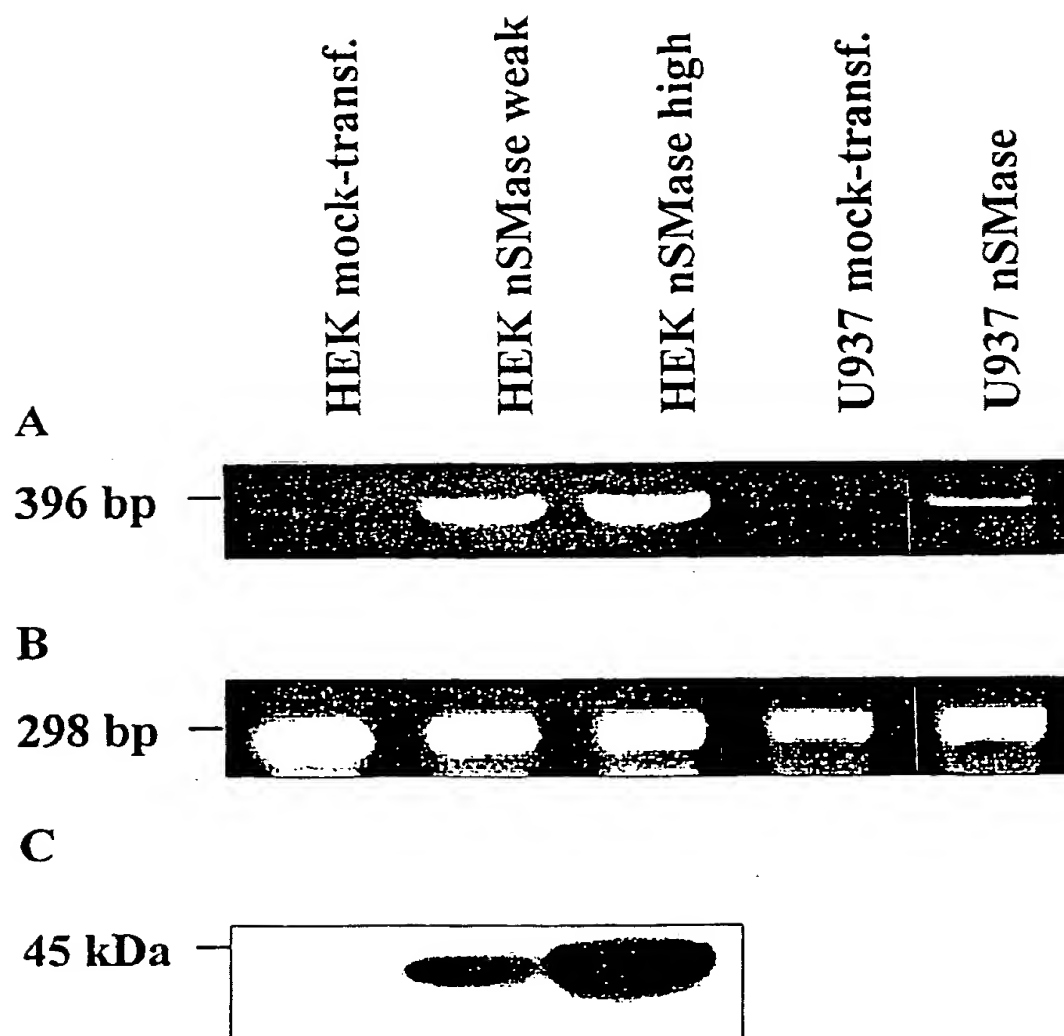
4321 AAANNTTCCCTNGGAAANCCCTTGNTTGGNAAAACCNAAATNANGAACCAANGCCAANNNT 4380
TTTNNAAGGGANCCTTTNGGGGAACNAACCNTTTGGNTTANTNCTTGGTNCGGTTNNA

4381 TGCCAANAAACCNTTTGGGCAAAGGGGGNAAATTCANCAANGGGGNAATTGGGGAAACCC 4440
ACGGTTNTTTGGNAAACCCGTTTCCCCCNTTTAAGTNGTTNCCCCNTTAACCCCTTTGGG

4441 NTGGGTTTNCCTCAAAGGGGCCNAANANT 4468
NACCCAAANGGGTTTCCCGGGNTTNTNA



FIG. 3





mnSMase "konventional" Knock Out

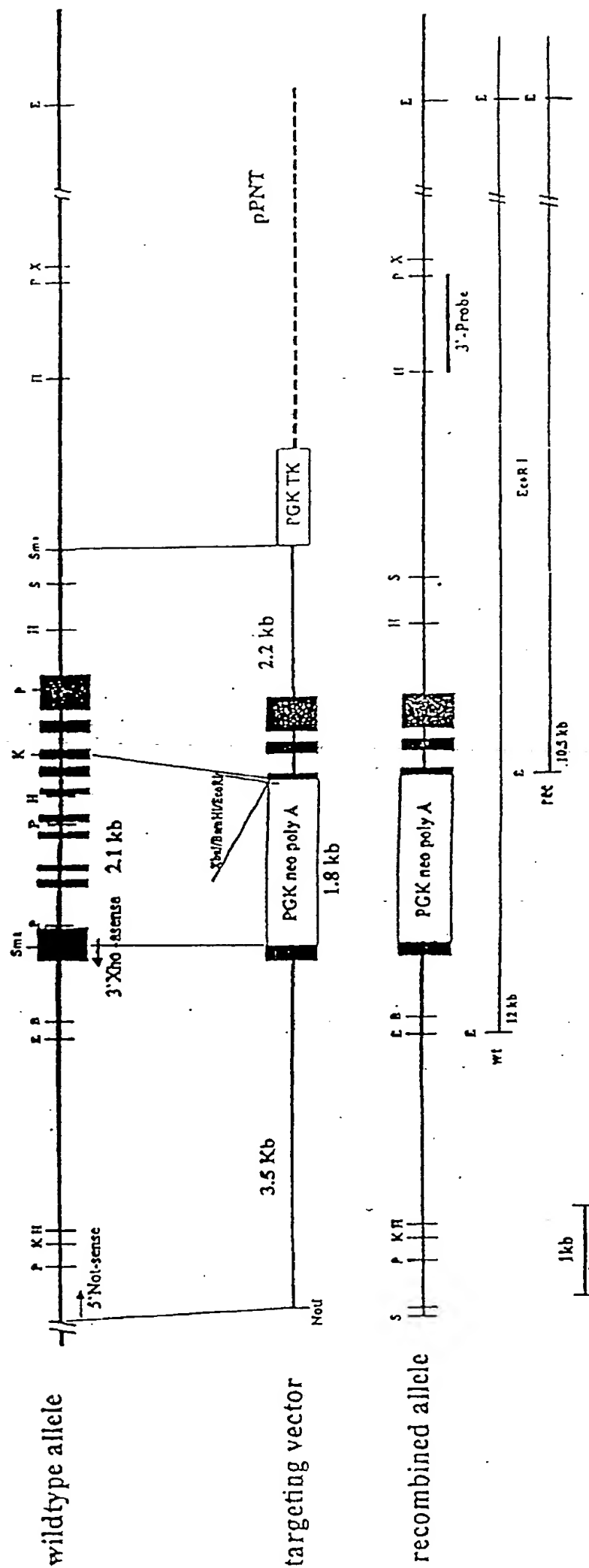




FIG. 5

Constructs for generating transgenic mouse mutants

ubiquitin promoter	nSMase	IRES	lacZ	polyA

polyA	rtTA	CMV	CMV-1	nSMase	IRES	GFP	polyA

Ubiquitin promoter: regulatory sequence of the ubiquitin gene, controlling a ubiquitous transcription.

nSMase: neutral sphingomyelinase

lacZ: lacZ, gene coding for β -galactosidase

polyA: recognition signal for the termination of transcription and polyadenylation

CMV: cytomegalovirus promoter of the cytomegalovirus gene, controlling a ubiquitous transcription.

rtTA: reverse transactivator, binds to the minimal promoter and thus controls transcription. The binding properties of the transactivator are influenced by tetracyclin. The addition of tetracyclin makes the transactivator bind to the minimal promoter and starts transcription, removal of tetracyclin prevents the binding of the transactivator to the minimal promoter and prevents transcription.

CMV-1: minimal promoter, binding of transactivator starts transcription.

IRES: *internal ribosomal entry sequence*, viral initiation signal for translation.